L10 ANSWER 1 OF 77 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2000:210509 CAPLUS
DOCUMENT NUMBER: 132:250017
TITLE: **Apoptosis marker** antibodies and methods of use
INVENTOR(S): Riss, Terry
PATENT ASSIGNEE(S): Promega Corporation, USA
SOURCE: PCT Int. Appl., 66 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE	
WO 2000017648	A1	20000330	WO 1999-US22262	19990924	<--
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM					
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG					
AU 9961629	A1	20000410	AU 1999-61629	19990924	<--
EP 1116029	A1	20010718	EP 1999-948459	19990924	
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO					
US 6350452	B1	20020226	US 1999-445615	19991208	
US 2002102268	A1	20020801	US 2001-11321	20011203	

PRIORITY APPLN. INFO.:
US 1998-101920P P 19980924
WO 1999-US22262 W 19990924
US 1999-445615 A3 19991208

AB Disclosed are antibodies that specifically recognize the new amino terminus of a protein cleaved by a protease during apoptosis. Methods of using and making the antibodies are also provided. The antibodies are particularly useful in methods of detecting apoptosis and testing candidate compds. for enhancing or inhibiting apoptosis.

REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE

FORMAT

L10 ANSWER 2 OF 77 MEDLINE DUPLICATE 1

L10 ANSWER 49 OF 77 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1998:15913 CAPLUS
DOCUMENT NUMBER: 128:84388
TITLE: Apurinic/apyrimidinic endonuclease (APE) as **marker** of (pre)**malignant** conditions and **apoptosis**, APE in monitoring of **cancer** therapy, and modulation of APE activity in **cancer** treatment
INVENTOR(S): Kelley, Mark R.; Duguid, John R.; Eble, John N.
PATENT ASSIGNEE(S): Advanced Research + Technology Institute, USA; Kelley, Mark R.; Duguid, John R.; Eble, John N.
SOURCE: PCT Int. Appl., 166 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE	
WO 9747971	A1	19971218	WO 1997-US10078	19970611	<--
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TR, TT, UA, UG, US, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM					
RW: GH, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG					
AU 9733865	A1	19980107	AU 1997-33865	19970611	<--
EP 923738	A1	19990623	EP 1997-929914	19970611	<--
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO					

PRIORITY APPLN. INFO.: US 1996-19561P P 19960611
US 1996-19602P P 19960611
WO 1997-US10078 W 19970611

AB Disclosed are methods and compns. for identifying, monitoring and treating premalignant and **malignant** conditions in a human subject. The present invention further discloses methods and compns. for detg. cells undergoing apoptosis, and for increasing the efficacy of a **cancer** therapy. The methods involve the use of apurinic/apyrimidinic endonuclease (APE), independently, as a marker for (pre)**malignant** conditions and for apoptosis. Also described are polyclonal antibody prepns. for use in methods for detecting APE and methods for modulating expression susceptibility of cells to apoptosis. Thus, an elevated level of APE was found to indicate a premalignant or **malignant** state of a cell in squamous cell **carcinoma** of the cervix. Decreased APE correlated with cells undergoing and/or likely to undergo apoptosis. To monitor the efficacy of a **cancer** therapy the therapeutic agent is administered to the **cancer** cells and the APE levels are subsequently detd. Decreased APE levels (as compared to pretreatment levels) indicates the cells are undergoing apoptosis and that the therapy is effective.

L11 ANSWER 4 OF 4 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1997:296001 CAPLUS
DOCUMENT NUMBER: 126:311835
TITLE: Apoptosis as a measure of chemosensitivity to cisplatin and Taxol therapy in ovarian cancer cell lines
AUTHOR(S): **Gibb, Randall K.**; Taylor, Douglas D.; Wan, Tina; O'connor, Dennis M.; Doering, David L.; Gercel-Taylor, Cicek
CORPORATE SOURCE: Department of Obstetrics and Gynecology, Division of Gynecological Oncology, University of Louisville School of Medicine, Louisville, KY, 40292, USA
SOURCE: Gynecologic Oncology (**1997**), **65** (1), **13**-22
CODEN: GYNOA3; ISSN: 0090-8258
PUBLISHER: Academic
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Cisplatin- and Taxol-induced apoptosis was studied in 4 human ovarian cancer cell lines to evaluate apoptosis as a measure of chemosensitivity. In vitro sensitivities of OVCAR-3, SKOV-3, UL-1, and UL-2 cells to cisplatin or Taxol were detd. by the sulforhodamine B assay. Induction of apoptosis was studied by DNA fragmentation following treatment with cisplatin and/or Taxol after 24- and 48-h exposure. DNA fragmentation was further quantitated by the diphenylamine assay, and the proportion of cells in the G1, G2/M, and S phases of the cell cycle was detd. by flow cytometry. Presence of the p53 gene product was examd. by Western blotting. The 4 cell lines represent various sensitivities to cisplatin and Taxol (LC50 range for cisplatin, 5-30 .mu.g/mL; Taxol, 30-1000 nM). UL-2 represents a resistant cell line which was 10-30 times more resistant to Taxol and 6 times more resistant to cisplatin than the other lines. Demonstration of apoptosis correlated with the sensitivity to both cisplatin and Taxol in cell lines OVCAR-3 and UL-2. DNA fragmentation in OVCAR-3 was uniformly present after 24 or 48 h when treated with cisplatin or Taxol. UL-2 demonstrated no apoptosis after 24 or 48 h of treatment with either cisplatin or Taxol. When sequencing expts. were performed, DNA fragmentation correlated with the cytotoxicity assays, except in UL-1 cells, where no difference was obsd. Pretreatment with Taxol generally resulted in enhanced cytotoxicity in a schedule-dependent manner, and increased fragmentation was demonstrated; cisplatin pretreatment consistently resulted in decreased fragmentation. Quantitation of the fragmented DNA correlated with that seen on gel electrophoresis. OVCAR-3 and UL-1 demonstrated the greatest change from basal values after 24 h, whereas UL-2 had little change following treatment. G1 arrest occurred more readily in OVCAR-3 and SKOV-3 than in the other cells. UL-2 cells had very little change in the proportion of cells entering G1 arrest, but had a significant increase in the G2/M proportion. In OVCAR-3, UL-1, and UL-2 cells, the presence of an aberrantly expressed p53 gene product was demonstrated, while no p53 was detected in the SKOV-3 cells. The findings indicate that the ability to achieve significant cytotoxicity by cisplatin and Taxol may be directly related to the induction of apoptosis; however,

cellular and genetic characteristics det. the eventual outcome of these treatments.

L18 ANSWER 53 OF 59 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2000:202075 CAPLUS
DOCUMENT NUMBER: 133:206093
TITLE: Apoptosis, bcl-2 Expression, and Proliferation in Benign and **Malignant** Endometrial Epithelium: An Approach Using Multiparameter Flow Cytometry
AUTHOR(S): Morsi, Hassan M.; Leers, Mathie P. G.; Radespiel-Troger, Martin; Bjorklund, Viveka; Kabarity, Hamdi El; Nap, Marius; Jager, Wolfram
CORPORATE SOURCE: Department of Obstetrics and Gynecology, Friedrich Alexander University, Erlangen, 91054, Germany
SOURCE: Gynecologic Oncology (**2000**), 77(1), 11-17
CODEN: GYNOA3; ISSN: 0090-8258
PUBLISHER: Academic Press
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Disturbances in the regulation of cell proliferation and differentiation play an important role in the formation of **neoplastic** lesions. Consequently, abnormalities in apoptosis regulation may contribute to this process. Expression of a neoepitope on cytokeratin 18, unmasked by an early caspase cleavage event and recognized by the novel monoclonal **antibody** M30, is an indicator of early epithelial cell apoptosis. The purpose of this study was to evaluate the quant. relation among apoptosis (M30), cell persistence (bcl-2), and proliferation (S-phase fraction; SPF) in **malignant** and benign endometrium. Using multiparameter DNA flow cytometry on 54 formalin-fixed paraffin-embedded samples from benign (proliferative, secretory, inactive, and hyperplastic endometrium) and **malignant** (grades 1-3 endometrial **adenocarcinoma**) endometrial tissue, bcl-2 expression and M30 reactivity were assessed together with the SPF in the cytokeratin-pos. epithelial cells. Benign cyclic endometrium showed a relatively high bcl-2 expression and low M30 reactivity in the proliferative phase whereas in the secretory phase this relation was inverse. In endometrial hyperplasia the expression of bcl-2 was increased compared to that in secretory and postmenopausal endometrium, but still below the level of proliferative samples. The expression of M30 also increased compared to normal proliferative endometrium but did not reach the level of endometrium in the secretory phase of the menstrual cycle. In **cancer** the expression of bcl-2 decreased with the progression of differentiation grade. For M30 expression this relation was inverse. Overall there was a significant increase of M30 reactivity in **cancerous** compared to hyperplasia and normal cyclic endometrium.Conclusion. Transition of endometrial epithelium from hyperplasia to **cancer** seems to involve both increased apoptosis and decreased bcl-2 expression. Flow cytometric evaluation of M30 and bcl-2 expression levels, with the SPF, in currettage specimens from postmenopausal patients complaining of bleeding provides a quant. assessment of endometrial apoptosis, anti-apoptosis, and proliferation. Further studies are needed to det. the relationship among these three processes as indicators of the biol. behavior of gynecol. **tumors**. (c) 2000 Academic Press.

L18 ANSWER 54 OF 59 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1999:330464 CAPLUS
DOCUMENT NUMBER: 130:335026
TITLE: Biochemical methods for detecting cervical dysplasia and **cancer**
INVENTOR(S): Smith-McCune, Karen; Grossnickle, Ellen Beth; Razani, Nooshin
PATENT ASSIGNEE(S): The Regents of the University of California, USA
SOURCE: PCT Int. Appl., 19 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE	
WO 9924620	A1	19990520	WO 1998-US23922	19981110	<--
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM					
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG					
CA 2309330	AA	19990520	CA 1998-2309330	19981110	<--
AU 9913933	A1	19990531	AU 1999-13933	19981110	<--
AU 734226	B2	20010607			
EP 1030934	A1	20000830	EP 1998-957749	19981110	<--
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI					
US 6221623	B1	20010424	US 1998-189124	19981110	
JP 2001522983	T2	20011120	JP 2000-519612	19981110	

PRIORITY APPLN. INFO.: US 1997-65206P P 19971110
WO 1998-US23922 W 19981110

AB Primary screening for cervical dysplasia is effected by measuring a biochem. **marker** of **apoptosis** and/or angiogenesis in each of a population of cells derived from convenient, superficial swabbing, sponging, scraping or lavage of superficial epithelial cells from the cervix, wherein the marker indicates the presence of cervical dysplasia in the sample, and scoring the results of the measuring step for cervical dysplasia (i.e. ascertaining whether or not the marker is present) in the patient in the absence of any cytol. examn.

REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L18 ANSWER 54 OF 59 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1999:330464 CAPLUS
DOCUMENT NUMBER: 130:335026
TITLE: Biochemical methods for detecting cervical dysplasia and **cancer**
INVENTOR(S): Smith-McCune, Karen; Grossnickle, Ellen Beth; Razani, Nooshin
PATENT ASSIGNEE(S): The Regents of the University of California, USA
SOURCE: PCT Int. Appl., 19 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9924620	A1	19990520	WO 1998-US23922	19981110 <--
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
CA 2309330	AA	19990520	CA 1998-2309330	19981110 <--
AU 9913933	A1	19990531	AU 1999-13933	19981110 <--
AU 734226	B2	20010607		
EP 1030934	A1	20000830	EP 1998-957749	19981110 <--
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
US 6221623	B1	20010424	US 1998-189124	19981110
JP 2001522983	T2	20011120	JP 2000-519612	19981110

PRIORITY APPLN. INFO.: US 1997-65206P P 19971110
WO 1998-US23922 W 19981110

AB Primary screening for cervical dysplasia is effected by measuring a biochem. **marker** of **apoptosis** and/or angiogenesis in each of a population of cells derived from convenient, superficial swabbing, sponging, scraping or lavage of superficial epithelial cells from the cervix, wherein the marker indicates the presence of cervical dysplasia in the sample, and scoring the results of the measuring step for cervical dysplasia (i.e. ascertaining whether or not the marker is present) in the patient in the absence of any cytol. examn.

REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L18 ANSWER 55 OF 59 CAPLUS COPYRIGHT 2003 ACS

L18 ANSWER 56 OF 59 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1997:147262 CAPLUS
DOCUMENT NUMBER: 126:207792
TITLE: Immunolocalization of EGF receptor (EGFr) in intestinal epithelium: recognition of apoptotic cells
AUTHOR(S): Booth, C.; Potten, C. S.
CORPORATE SOURCE: CRC Department of Epithelial Biology, Paterson Institute, Christie Hospital NHS Trust, Manchester, M20 9BX, UK
SOURCE: Apoptosis (**1996**), 1(3), 191-200
CODEN: APOPFN; ISSN: 1360-8185
PUBLISHER: Rapid Science Publishers
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The EGF-like family of growth factors are known to be involved in the control of the intestinal epithelium. The intracellular events are mediated by the EGF receptor (EGFr), a transmembrane glycoprotein which is overexpressed in many **malignancies** and also in many radiosensitive cell types. The precise mode of action of the receptor in controlling proliferation and whether the factor is also involved in controlling apoptosis in this tissue is not clear. Using polyclonal **antibodies** raised against a cytoplasmic region of the receptor distant to the phosphorylation site and one raised against the peptide sequence DVVDADEYLIPQ, which is present in the cytoplasmic tail phosphorylation site of the EGFr, the authors examd. the immunostaining in normal and irradiated murine intestine. The former **antibody** labeled the basolateral membranes of the epithelial cells in the proliferative zones of both the small intestine and colon, in both control and irradiated tissue. The latter **antibody** however, strongly labeled the Goblet cells and the microvilli of the enterocyte apical membrane in control tissue. Following irradn. the apical labeling redistributed and was localized in the apical cytoplasm and in a paranuclear region. Furthermore, strong labeling was now seen in many of the apoptotic cells of the small intestinal epithelium. The greatly differing results with the two **antibodies** indicates that interpretation of such immunostaining must be viewed with caution and may relate to the availability of each particular epitope. These results also suggest that **antibodies** to DVVDADEYLIPQ may be a useful **marker** of **apoptotic** calls and could imply a correlation between high levels of epitope availability, the radiosensitive (frequently p53 expressing) cells of the crypt epithelium and the induction of apoptosis.